

**Results:** Leg extension muscle power increased  $29\% \pm 44$  (affected side) and  $19\% \pm 20$  (unaffected side) in IG compared to  $-3\% \pm 21$  (affected side) and  $-2\% \pm 20$  (unaffected side) in CG (between group comparison;  $p=0.0002$ ). Isometric hip extension force increased  $29\% \pm 35$  (affected side) and  $26\% \pm 21$  (unaffected side) in IG compared to  $-1\% \pm 16$  (affected side) and  $2\% \pm 18$  (unaffected side) in CG ( $p<0.0001$ ). Isometric knee extension force increased  $20\% \pm 27$  (affected side) and  $18\% \pm 21$  (unaffected side) in IG compared to  $-4\% \pm 16$  (affected side) and  $-5\% \pm 16$  (unaffected side) in group CG ( $p<0.0001$ ). There were no significant differences between groups regarding baseline levels of age, height, body weight, gender distribution or muscle function.

**Conclusions:** This randomized explorative trial showed that intervention with 10 weeks of progressive preoperative RT induced a significant gain in muscle power and isometric muscle force compared with controls in patients with end stage hip OA. This study holds promise to provide information on the potential postoperative advantage on outcome of progressive preoperative RT.

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### AN ORAL PREPARATION CONTAINING HYLAURONIC ACID (ORALVISC®) CAN REDUCE OSTEOARTHRITIS KNEE PAIN AND SERUM AND SYNOVIAL FLUID BRADYKININ

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**Purpose:** A leading cause of knee osteoarthritis disability is pain. Non steroidal, acetaminophen, and narcotics relieve pain but may have side effects. Injectable hyaluronic acid (HA) may down regulate inflammatory and biochemical pain pathways. Bradykinin is a known neurotransmitter for pain. Our purpose was to compare placebo to oral HA. The three hypotheses were: (1.) supplementation with oral HA would significantly improve knee pain and function over a 3 months period, (2.) clinical response to oral HA would be related to metabolic syndrome, and (3.) clinical response to oral HA would be related changes in serum and synovial fluid levels of bradykinin.

**Methods:** This was a prospective randomized double-blind placebo-controlled study comparing a patented oral HA (Oralvisc®) to placebo for the treatment of knee OA. At completion two placebo patients could not have arthrocentesis. All remaining data was available for 21 drug and 19 placebo patients. Subjects were between 50-75 years old, had OA based on imaging, a visual analog score (VAS)  $>50$  mm, and an effusion where a joint aspiration or intra-articular injection would be clinically indicated. Exclusion included recent trauma, any inflammatory joint disorder, recent surgery, severe comorbidities, recent intra-articular injections, and oral or topical corticosteroids. 576 patients were screened and 51 recruited and randomized. 3 drug patients did not return and 1 had surgery. 3 placebo patients did not return and 3 had enrollment errors. All patients took their preparation daily for 3 months. They were evaluated monthly for VAS and WOMAC pain and joint function. Serum and synovial fluid was collected at the beginning and at 12 weeks. Bradykinin was measured by an ELISA. Patients were assessed each month for any unused capsules receiving capsules for the next four weeks. Initial body mass index (BMI), metabolic score (MS) 0 - 4, MRI changes, Kellgren-Lawrence (KL) scores, age, race, and sex were reviewed for the two groups. Repeated measures analyses were used for all clinical comparisons including pain and function scores as well as BMI. There were no restrictions on other pain medications or therapies.

**Results:** Demographics, BMI, and KL scores were even for both groups. The initial high VAS for placebo was  $6.18 \pm 0.24$  cm and for drug was  $6.75 \pm 0.28$  cm. After 3 months, the values fell to  $5.84 \pm 0.76$  cm and  $4.06 \pm 0.85$  cm respectively ( $p=0.0035$ ). The initial high WOMAC pain score for placebo was  $8.05 \pm 1.17$  and for drug was  $8.81 \pm 0.81$ . After 3 months the score rose to  $8.16 \pm 1.13$  for placebo and fell to  $5.79 \pm 1.34$  for the drug group ( $p=0.0259$ ). The initial WOMAC function score was  $40.53 \pm 5.18$  for placebo and  $40.29 \pm 3.07$  for drug. After 3 months of treatment, the score was reduced by 31% ( $27.62 \pm 7.44$ ) for the drug group but maintained for placebo ( $39.58 \pm 6.17$ ), resulting in statistical differences between treatment groups ( $p=0.0132$ ). The reduction in VAS score ( $p=0.0098$ ) WOMAC pain ( $p=0.0121$ ) and WOMAC function ( $p=0.0169$ ) was significant for those taking HA but not for those taking placebo ( $p < 0.05$ ), showing significant differences on the time evolution of the studied parameters. The final serum bradykinin levels were significantly lower for oral HA, 144 pg versus placebo 151 pg ( $p <$

0.05) with synovial fluid decrease significantly more for oral HA, 61 pg, versus placebo -29 pg ( $p < 0.05$ ). Change in bradykinin was inversely related to MS.

**Conclusions:** Intra-articular HA may improve the symptoms of OA by mitigating the activities of proinflammatory mediators and pain producing neuropeptides released by activated synovial cells. Bradykinins participate in innate immunity, inflammation, and pain. Chondrocyte receptors increase interleukin on stimulation. The relationship of reduction of bradykinin and decreased pain in the oral HA group is consistent with the role of bradykinin in joint pain. Further research will be required to determine how this very promising agent leads to changes in bradykinin levels.

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### DEVELOPING A QUESTIONNAIRE TO ASSESS THE BURDEN OF OSTEOARTHRITIS

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**Purpose:** The Global Burden of Disease (GBD) was initially described in the 1990s by the WHO as a “health gap”. This concept was particularly useful for quantifying a population’s health and determining public health action priorities. Today the notion of a burden goes beyond the idea of a “health gap”, and it is common to assess 2 types of burden for chronic diseases: the global burden (assessment of the economic impact of disease management for society as a whole and especially for the payee) and the individual burden (handicap assessment, in the largest sense of the term, as caused by the disease).

The goal was to develop a tool to measure the handicap of this chronic condition on patients’ daily life in the largest sense of the term (psychological, social, economic, and physical impact).

**Methods:** The questionnaire was developed in 3 phases: exploratory, development, and validation (figure 1). A multidisciplinary team (general practitioners, rheumatologists, patient associations, quality of life experts) was involved throughout the entire rigorous methodological process. These players, working in patient treatment or with expertise in questionnaire development, made it possible to guarantee the clinical and scientific applicability of the tool.

**Results: Exploratory phase:** An in-depth literature review concluded that there are many different assessment tools used for osteoarthritis. Some focus on a single joint (hip, knee, hand) or on pre/post prosthetics attachment. Others were developed for very specific diseases (such as rheumatoid arthritis) and do not concern osteoarthritis. The available questionnaires do not cover certain fields such as the psychological and aesthetic impacts of the disease, sufficiently or at all, even though the latter is one of the primary causes of complaint.

In order to ensure the participation of patients with diverse profiles, arthritic patients contributing to the question wording were recruited by rheumatologists working privately or in hospitals, GP and patient associations. In total, 130 subjects with osteoarthritis discussed their complaints and handicaps related to osteoarthritis.

Following qualitative interviews, the main statements received were: discouragement when dealing with the condition, difficulty completing simple daily activities, changes in physical appearance, and the view of arthritis as a handicap. Altered family interaction was emphasized over altered interaction with others. At this stage 56 items were organized to generate 41 questions.

**Development phase:** The wording of possible answers was set. An initial assessment made it possible to limit redundancy by grouping similar questions. Indiscernible questions were also removed. The pilot version of the questionnaire consisted of 25 questions, making it easier to use in large-scale longitudinal studies.

Finally, a specialized institution used cognitive debriefing to ensure that each question was well-understood by and acceptable to patients. This step did not bring about any major changes in question wording.

**Conclusions:** This new questionnaire must undergo psychometric validation before it can be used (for internal and external validity)\*. A factorial analysis would also be necessary to bring out the latent characteristics measured by this questionnaire and identify the items that are highly - or too closely - correlated between them. Finally, a scoring system will be set to facilitate interpretation of the overall handicap imposed by osteoarthritis on patients’ daily lives.